

US EPA ARCHIVE DOCUMENT

DP Barcode :D186631  
PC Code No. :112701  
EFGWB Out :

JUL 12 1993

TO: Barbara Briscoe  
Product Manager PM 51  
Special Review and Reregistration (H7508W)

FROM: Akiva Abramovitch, Ph.D., Head  
Environmental Chemistry Review Section #3  
Environmental Fate & Ground Water Branch/EFED (H7507C)

THRU: Henry Jacoby, Chief  
Environmental Fate & Ground Water Branch/EFED (H7507C)

Attached, please find the EFGWB review of...

Reg./File # :2755

Common Name :Brodifacoum

Product Name :Talon, Havoc

Company Name :ICI Americas, Inc.

Purpose :Review of 162-1 and 163-1 studies for reregistration

Type Product :Rodenticide Action Code: 603 EFGWB #(s): 93-0312 Review Time: 1.0 days

EFGWB Guideline/MRID/Status Summary Table: The review in this package contains...

161-1		162-4		164-4		166-1	
161-2		163-1	42568301	Y	164-5		166-2
161-3		163-2		165-1			166-3
161-4		163-3		165-2			167-1
162-1	42579401	N	164-1		165-3		167-2
162-2		164-2		165-4			201-1
162-3		164-3		165-5			202-1

Y = Acceptable (Study satisfied the Guideline)/Concur P = Partial (Study partially satisfied the Guideline, but additional information is still needed)  
S = Supplemental (Study provided useful information, but Guideline was not satisfied) N = Unacceptable (Study was rejected)/Non-Concur

\* \* \* DATA PACKAGE INFORMATION \* \* \*

DP BARCODE: 186631 EXPEDITE: N DATE SENT: 01/12/93 DATE RET.: / /  
 CHEMICAL: 112701 Brodifacoum  
 DP TYPE: 999 Miscellaneous Data Package  
 ADMIN DUE DATE: 05/12/93 CSF: LABEL:  
 ASSIGNED TO DATE IN DATE OUT  
 DIV : EFED 01/12/93 / /  
 BRAN: EFGB / /  
 SECT: / /  
 REVR : / /  
 CONTR: / /

\* \* \* DATA REVIEW INSTRUCTIONS \* \* \*

Please review the attached data package for study 162-1 and 163-1, 425794-01 and 425683-01.

\* \* \* ADDITIONAL DATA PACKAGES FOR THIS SUBMISSION \* \* \*

DP BC	BRANCH/SECTION	DATE OUT	DUE BACK	INS	CSF	LABEL
155537	EEB/RS1	09/11/90	10/02/90	Y	N	N
155538	EFGB/CRS3	09/11/90	10/02/90	Y	N	N
155539	OREB/IO	09/11/90	10/02/90	Y	N	N
155540	TB-2	09/11/90	10/02/90	Y	N	N
155541	OREB/RS-1	09/11/90	10/02/90	Y	N	N
156104	EEB/RS1	09/26/90	10/17/90	Y	N	N
156105	TB-2	09/26/90	10/17/90	Y	N	N
158516	TB-2	11/21/90	12/12/90	Y	N	N
159541	RSB/IO	12/17/90	01/07/91	Y	N	N
159610	EFGB/IO	12/19/90	01/09/91	Y	N	N
170786	EEB	11/04/91	12/04/91	Y	N	N
170787	EEB	11/04/91	12/04/91	Y	N	Y
170790	TB-2/RS-2	11/04/91	12/04/91	Y	N	Y
172556	TB-2	12/23/91	01/22/92	Y	N	Y
186599	EFGB	01/12/93	05/12/93	Y	N	Y
186628	EFGB	01/12/93	05/12/93	Y		

2

DP BARCODE: D186631

CASE: 816404  
SUBMISSION: S381755

DATA PACKAGE RECORD  
BEAN SHEET

REREG CASE # 275

DATE: 01/12/9  
Page 1 of 1

\* \* \* CASE/SUBMISSION INFORMATION \* \* \*

CASE TYPE: REREGISTRATION ACTION: 603 RESUBMISSION  
CHEMICALS: 112701 Brodifacoum

100.00

ID#: 112701-010182  
COMPANY: 010182 ICI AMERICAS INC  
PRODUCT MANAGER: 51 BARBARA BRISCOE  
PM TEAM REVIEWER: FRANKLIN RUBIS  
RECEIVED DATE: 09/11/90 DUE OUT DATE: / /

703-308-8177  
703-308-8184

ROOM: CS1 3H3  
ROOM: CS1 4L5

1. CHEMICAL:    Common name:

Brodifacoum.

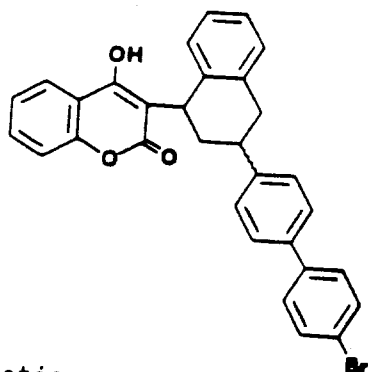
Chemical name:

3-[3-(4'-Bromo-1,1'-biphenyl-4-yl)-1,2,3,4-tetrahydro-1-naphthyl]-4-hydroxycoumarin.

Trade name(s):

Talon, Havoc.

Structure:



Formulations:

Ready-to-use grain-base in pellets, mini pellets, and wax blocks.

Physical/Chemical properties:

Molecular formula:  $C_{31}H_{23}BrO_3$ .  
Molecular weight: 523.4.  
Physical state: Off-white powder.  
Melting point: 228-232 C.  
Vapor pressure (25 C): <0.13 mPa.  
Solubility (20 C): <10 mg/L water at pH 7; 6-20 g/L acetone; <0.6-6.0 mg/L benzene; 3 g/L chloroform.

2. TEST MATERIAL:

Study 1 and 2: Active ingredient.

3. STUDY/ACTION TYPE:

Review of aerobic soil metabolism and mobility (aged column leaching) studies.

4. STUDY IDENTIFICATION:

162-1: Aerobic Soil Metabolism

Hall, B.E., and I. Priestly. 1992. Brodifacoum: Metabolism in soil under aerobic conditions. Laboratory Project ID: 381441. Unpublished study performed by Inveresk Research International, Tranent, Scotland, and submitted by ICI Americas Inc., Wilmington, DE. (42579401)

163-1: Mobility/Aged Column Leaching

Jackson, R., and B.E. Hall. 1992. Aged soil leaching of [ $^{14}\text{C}$ ]brodifacoum. Laboratory Project ID: 381986. Unpublished study performed by Inveresk Research International, Tranent, Scotland, and submitted by ICI Americas Inc., Wilmington, DE. (42568301)

5. REVIEWED BY:

David Edelstein  
Soil Scientist  
EFGWB/EFED/OPP  
Review Section #3

Signature: David Edelstein

Date: July 6, 1993

6. APPROVED BY:

Akiva Abramovitch  
Chief  
EFGWB/EFED/OPP  
Review Section #3

Signature: Akiva Abramovitch

Date: JUL 6 1993

7. CONCLUSION:

162-1: Aerobic Soil Metabolism (MRID 42579401; unacceptable at this time)  
Brodifacoum degraded with a half-life of 157 days in sandy clay loam soil incubated in the dark at 21 C and 75% of 0.33 bar moisture capacity. No nonvolatile degradates other than  $^{14}\text{CO}_2$  were identified;  $^{14}\text{CO}_2$  comprised 36% of the applied radioactivity at 52 weeks posttreatment. Up to eleven [ $^{14}\text{C}$ ]compounds other than [ $^{14}\text{C}$ ]brodifacoum were isolated from the soil extracts at 2.07 to 17.34% of the applied (0.008 to 0.067 ppm), but none were identified. In order for this study to fulfill the aerobic soil metabolism data requirement, all [ $^{14}\text{C}$ ]compounds isolated from the soil at  $\geq 0.01$  ppm must be identified, especially compounds D, E, F, and K. Additional information may be required on the aerobic soil metabolism of brodifacoum labeled in other positions of the molecule.

163-1: Mobility/Aged Column Leaching (MRID 42568301; acceptable)

Based on column leaching experiments, aged (30 days) brodifacoum residues (89-97% as brodifacoum) were relatively immobile in columns of sand, sandy clay loam, silty clay, or clay soils from Great Britain that were leached with 20 inches of 0.01 M calcium chloride solution. Following leaching, 78.81-94.87% of the applied radioactivity remained in the layer of aged soil and  $\leq 0.32\%$  was recovered in the leachate. No degradates were identified in the soil or leachate. Degradates examined in this study included "A" and "C" from the aerobic metabolism study. Mobility data

(either batch equilibrium or column leaching) will also be required for degradates "D," "E," "F," and "K," the major degradates in the aerobic soil metabolism study. Because so little degradation was observed, this study will be considered as fulfilling the unaged mobility data requirement. Additional data will be needed on the mobility of brodifacoum degradates in order to satisfy the aged mobility data requirement.

#### ENVIRONMENTAL FATE ASSESSMENT

Brodifacoum appears to be a relatively persistent chemical. Results from hydrolysis studies were not reliable (MRID 42237701; reviewed 11/9/92), and could not be used to calculate a half-life. Brodifacoum has a long aerobic soil metabolism half-life of 157 days. As many as six degradates were separated on a single TLC plate following the aerobic soil experiment. As these degradates have not been characterized or identified, it is not yet possible to say whether each TLC spot represented a distinct compound.

A column leaching study of brodifacoum aged 30 days in four British soils demonstrated that brodifacoum is immobile in soil. However, several of the major brodifacoum degradation products do not reach a significant concentration until one half-life has been completed. Additional mobility data will be needed for these degradates.

#### 8. RECOMMENDATIONS:

Inform the registrant that:

- 1) The Phase IV Review of brodifacoum (EFGWB #90-0881) of 11/19/90 states that the data requirements imposed for brodifacoum are hydrolysis, aerobic soil metabolism, and mobility (adsorption/desorption or leaching).
- 2) The hydrolysis and aerobic soil metabolism studies must be repeated with sufficient analytical rigor to identify all degradates present at concentrations greater than 10% of the applied or 0.01 ppm, whichever is smaller, as well as any change in the distribution of brodifacoum between the cis and trans isomers.
- 3) Although the mobility study accepted here was described as an aged column leaching study, it does not fully satisfy the aged mobility data requirement for brodifacoum. The test material was aged for 30 days, but the major brodifacoum degradates had not yet formed. However, because parent brodifacoum was essentially intact throughout the study, the data submitted here do fulfill the unaged mobility requirement for brodifacoum. Additional mobility studies are required on the mobility of major degradates.
- 4) If batch equilibrium is performed, a preliminary study will be necessary to determine the maximum solubility of brodifacoum degradates in 0.01 N  $\text{CaCl}_2$  solution. Test concentrations should not exceed this maximum solubility. Studies on at least four U.S. soils are required.

5) If column leaching studies are performed, at least two, and preferably four, U.S. soils must be used. European soils should not be used, as the accepted column leaching study was done entirely in British soil.

6) Mobility data will be required for all major degradates, either as batch equilibrium with each individual degradate or as an aged soil column leaching study including at least two U.S. soils.

9. BACKGROUND:

A. Summary of Previously Reviewed Data

1) 161-1: Hydrolysis: (MRID 42237701; unacceptable)

These data are considered to be of uncertain value and should not be used to predict the environmental behavior of brodifacoum residues. This study is unacceptable because brodifacoum degradates were not adequately identified and evidence of storage stability was not provided although samples were stored frozen before analysis. Brodifacoum appeared to degrade rapidly for 24 hours at pH 5, 7 and 9, but no degradation was observed after that time. No explanation was offered for this unusual chemical behavior aside from the admission of possible methodology problems. It is unlikely that all of these problems can be resolved, and a new study will be required.

2) 163-1: Mobility-Adsorption/Desorption: (MRID 42024501; unacceptable)

These data are considered to be of uncertain value and should not be used to predict the environmental behavior of brodifacoum residues. This study is unacceptable because acetone was used as a co-solvent, resulting in brodifacoum concentrations far in excess of possible concentrations in the field. Brodifacoum is soluble in acetone at up to 20,000 ppm. Brodifacoum was applied to a 2 g soil/20 ml water slurry at 0.9-4.5 ppm, although the study author stated that Brodifacoum solubility in water is <0.1 ppm in 0.01 N CaCl<sub>2</sub> solution. It is not possible to extrapolate these results into realistic solubility ranges, or to discount the likelihood that Brodifacoum was partitioned out of the aqueous solution and into the acetone co-solvent. In addition, Freundlich K values were not calculated.

B. Directions for Use

Brodifacoum is an anticoagulant rodenticide registered for use to control Norway rats, roof rats, and house mice (including warfarin resistant strains) in public, industrial, farm, and commercial buildings. Brodifacoum may also be used in residential and urban indoor/outdoor areas by professional pest control personnel. Single active ingredient formulations include ready-to-use grain-base bait in pellets, mini pellets, and wax blocks.

10. DISCUSSION OF INDIVIDUAL TESTS OR STUDIES:

Refer to attached reviews.



11. COMPLETION OF ONE-LINER:

The one-liner has been updated and is attached.

12. CBI APPENDIX:

All data reviewed here are considered "company confidential" by the registrant and must be treated as such.

DATA REQUIREMENT STATUS: BRODIFACOU (RESIDENTIAL/INDUSTRIAL OUTDOOR USE)

GUIDELINE	MRID #	EFGWB#	DATE	STATUS
HYDROLYSIS	42237701	92-0044	11/92	NOT SATISFIED
AEROBIC SOIL METABOLISM	42579401	93-0312	7/93	NOT SATISFIED
LEACHING/ ADSORPTION/ DESORPTION	42024501 42568301	92-0884 93-0312	11/92 7/93	NOT SATISFIED

# DATA EVALUATION RECORD

## STUDY 1

CHEM 112701

Brodifacoum

§162-1

FORMULATION--00--ACTIVE INGREDIENT

STUDY ID 42579401

Hall, B.E., and I. Priestly. 1992. Brodifacoum: Metabolism in soil under aerobic conditions. Laboratory Project ID: 381441. Unpublished study performed by Inveresk Research International, Tranent, Scotland, and submitted by ICI Americas Inc., Wilmington, DE.

DIRECT REVIEW TIME = 12

REVIEWED BY: L. Parsons  
TITLE: Staff Scientist  
ORG: Dynamac Corporation  
Rockville, MD  
TEL: 301-417-9800

APPROVED BY: D. Edelstein  
TITLE: Soil Scientist  
ORG: EFGWB/EFED/OPP  
TEL: 703-305-5935

SIGNATURE:

## CONCLUSIONS:

### Metabolism - Aerobic Soil

1. This study cannot be used to fulfill data requirements.
2. Brodifacoum degraded with a half-life of 157 days in sandy clay loam soil incubated in the dark at 21 C and 75% of 0.33 bar moisture capacity. No nonvolatile degradates other than  $^{14}\text{CO}_2$  were identified;  $^{14}\text{CO}_2$  comprised 36% of the applied radioactivity at 52 weeks posttreatment.
3. This study is scientifically sound, but does not meet Subdivision N data requirements for the following reason:  
up to eleven [ $^{14}\text{C}$ ]compounds other than [ $^{14}\text{C}$ ]brodifacoum were isolated from the soil extracts at 2.07 to 17.34% of the applied (0.008 to 0.067 ppm), but were not identified.

4. In order for this study to fulfill the aerobic soil metabolism data requirement, [ $^{14}\text{C}$ ] compounds isolated from the soil at  $\geq 0.01$  ppm must be identified. Additional information may be required on the aerobic soil metabolism of brodifacoum labeled in other positions of the molecule.

#### METHODOLOGY:

Sieved (2 mm) sandy clay loam soil (63.1% sand, 16.5% silt, 20.4% clay, 4.24% organic matter, pH 7.1, CEC 13.56 meq/100 g), was weighed (50 g dry weight) into 250-mL Erlenmeyer flasks and moistened with deionized water to 75% of 0.33 bar. After 5 days of acclimatization, the soil was treated at 0.38 ppm with [ $^{14}\text{C}$ ]brodifacoum (3-[3-(4'-bromobiphenyl-4-yl)-1,2,3,4-tetrahydro-1-naphthyl]-4-hydroxycoumarin; uniformly labeled in the phenyl ring of the hydroxycoumarin moiety; radiochemical purity 98.2%, specific activity 45.86 uCi/mg, ICI), dissolved in acetonitrile. The soils were mixed by tumbling, then the sample flasks were connected to a continuous air-flow system. Humidified,  $\text{CO}_2$ -free air was drawn through separate flasks, and the gases leaving the flasks were combined and passed sequentially through a polyurethane foam plug and ethanediol, 0.5 M sulfuric acid, and ethanalamine trapping solutions. The samples were incubated in the dark at 19-22.5 C, and the moisture content of the soils was maintained at 75% of 0.33 bar for the duration of the experiment. The foam plugs and trapping solutions were replaced weekly for the first 8 weeks, then either biweekly or when samples were removed for analysis through 52 weeks. Duplicate flasks of soil were collected for analysis immediately posttreatment; at 3, 7, 14, and 28 days; and at 8, 13, 17, 26, 39, and 52 weeks.

The soil samples were extracted twice with methylene chloride:methanol (4:1; v:v), first by shaking overnight on an orbital shaker, then for 2-3 hours using a wrist-action shaker. Following each extraction, the slurries were centrifuged and the supernatant removed. Portions of the extracted soils were analyzed for unextracted [ $^{14}\text{C}$ ]residues using LSC following combustion. Aliquots of the individual extracts from the 0-, 3-, and 7-day posttreatment samples were analyzed for total radioactivity using LSC; the two extracts from each sample were then combined for further analysis. For samples from later intervals, the two extracts were pooled into a single sample prior to analysis using LSC. Aliquots of the combined extracts were evaporated to dryness under a stream of nitrogen, and the resulting residues were redissolved in acetone and analyzed using one-dimensional TLC on silica gel plates developed in chloroform (100%; Solvent System 1), dioxan:petroleum ether (30:70, v:v; Solvent System 2), or toluene:propan-2-ol:acetic acid (9:1:1, v:v:v; Solvent System 3). All sample extracts were analyzed using Solvent System 1; extracts of samples from 0 days through 17 weeks were analyzed using Solvent System 2; and extracts of samples from 28 days and 17 through 52 weeks were analyzed using Solvent System 3. [ $^{14}\text{C}$ ]Residues on the plates were located and quantified using a linear scanner, and were

identified by comparison to the location of unlabeled brodifacoum and 4-hydroxycoumarin reference standards that had been cochromatographed with the samples and located using UV (254 nm) detection.

After the soil samples were removed, the incubation flasks were rinsed with acetone and the rinsate was analyzed by LSC. The polyurethane foam plugs were rinsed with acetonitrile, and the rinsates were analyzed for total radioactivity using LSC. Aliquots of the trapping solutions were analyzed using LSC.

#### DATA SUMMARY:

[<sup>14</sup>C]Brodifacoum (3-[3-(4'-bromobiphenyl-4-yl)-1,2,3,4-tetrahydro-1-naphthyl]-4-hydroxycoumarin; uniformly labeled in the phenyl ring of the hydroxycoumarin moiety; radiochemical purity 98.2%), at 0.38 ppm, degraded with a registrant-calculated half-life of 157 days (22.5 weeks) in silty clay loam soil that was incubated in the dark at 21 ± 2 C and moistened to 0.75% of 0.33 bar for 1 year. In duplicate samples, [<sup>14</sup>C]brodifacoum declined from 88.77-97.48% of the applied at 0 days posttreatment to 54.38-56.13% at 17 weeks, 38.60-40.23% at 26 weeks, and 15.96-17.91% at 52 weeks (sum of cis and trans isomers in Table 2; TLC with chloroform solvent). The trans isomer of [<sup>14</sup>C]brodifacoum degraded more rapidly than the cis isomer; the ratio of cis- to trans-[<sup>14</sup>C]brodifacoum changed from 41:52 immediately posttreatment to 12:5 at 52 weeks.

Using three different TLC solvent systems, possibly eleven different [<sup>14</sup>C]compounds were isolated from soil extracts but were not identified. Using chloroform as the solvent, degradate "A" (R<sub>f</sub> 0.05) was a maximum of 3.94% of the applied; degradate "B" (R<sub>f</sub> 0.09) was a maximum of 3.50%; degradate "C" (R<sub>f</sub> 0.20) was a maximum of 2.07%; degradate "D" (R<sub>f</sub> 0.43) was a maximum of 7.72%; and degradate "E" (R<sub>f</sub> 0.73) was a maximum of 16.07% (Table 2). Using dioxan:petroleum ether (30:70) as the solvent, degradate "F" (R<sub>f</sub> 0.30) was a maximum of 8.38% of the applied; degradate "G" (R<sub>f</sub> 0.35) was a maximum of 4.33%; degradate "H" (R<sub>f</sub> 0.44) was a maximum of 3.92%; and degradate "I" (R<sub>f</sub> 0.10) was a maximum of 4.51% (Table 3). Using toluene:propan-2-ol:acetic acid (9:1:1) as the solvent, degradate "J" (R<sub>f</sub> 0.52) was a maximum of 3.77% of the applied and degradate "K" (R<sub>f</sub> 0.69) was a maximum of 17.34% (Table 4).

Unextracted [<sup>14</sup>C]residues in the soil increased from 2.60-3.91% of the applied immediately posttreatment to 11.12-13.00% at 28 days and a maximum of 23.29-30.15% at 39 weeks (Table 1). <sup>14</sup>CO<sub>2</sub> was 21.41% of the applied at 26 weeks and 35.80% at 52 weeks; other volatile [<sup>14</sup>C]compounds totaled 1.85% of the applied at 52 weeks. During the study, material balances ranged from 96.63 to 108.88% of the applied.

COMMENTS:

1. Using three different TLC solvent systems, eleven [ $^{14}\text{C}$ ] compounds other than [ $^{14}\text{C}$ ] brodifacoum were isolated from the soil extracts at 2.07 to 17.34% of the applied (0.008 to 0.067 ppm, respectively). No attempt was made to identify the compounds that were isolated; therefore it was uncertain if the same compounds were isolated in more than one solvent system; the study authors suggested that degradates "E" and "K" may be the same compound. The only degradate for which a reference standard was cochromatographed was 4-hydroxycoumarin, which was never isolated. Subdivision N guidelines specify that degradates present at  $\geq 0.01$  ppm should be identified.
2. Although brodifacoum is a complex molecule, the degradates were not identified and a degradation pathway was not established. Depending on the proposed degradation pathway, additional information may be required using brodifacoum in which other portions of the molecule carry the radiolabel.
2. Radioactivity in the ethanolamine traps was assumed to be  $^{14}\text{CO}_2$ ; it did not appear that confirmatory techniques such as precipitation with barium chloride were performed.
3. In an attempt to extract additional radioactivity from the soil, portions of methylene chloride:methanol-extracted soil from the 8-, 13-, and 17-week sampling intervals were extracted once with methanol and twice with methanol:water, each time by shaking overnight on a wrist-action shaker. The extracts were analyzed for total radioactivity using LSC. An additional 1.20-2.31% of the applied was extracted with methanol, and an additional 0.77-1.34% was extracted with methanol:water.
4. In an ancillary experiment to determine microbial viability, additional flasks of soil were either treated with unlabeled brodifacoum or were left untreated. These samples were incubated with the soil treated with [ $^{14}\text{C}$ ] brodifacoum. The populations of microbes in the soil were measured at 26 and 53 weeks posttreatment, and no significant difference was observed between the treated and untreated soils.

---

Page \_\_\_\_\_ is not included in this copy.

Pages 14 through 25 are not included in this copy.

---

The material not included contains the following type of information:

- ☐ Identity of product inert ingredients.
- ☐ Identity of product impurities.
- ☐ Description of the product manufacturing process.
- ☐ Description of quality control procedures.
- ☐ Identity of the source of product ingredients.
- ☐ Sales or other commercial/financial information.
- ☐ A draft product label.
- ☐ The product confidential statement of formula.
- ☐ Information about a pending registration action.
- ☒ FIFRA registration data.
- ☐ The document is a duplicate of page(s) \_\_\_\_\_.
- ☐ The document is not responsive to the request.
- ☐ Internal deliberative information.
- ☐ Attorney-Client work product.
- ☐ Claimed Confidential by submitter upon submission to the Agency.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

---

# DATA EVALUATION RECORD

## STUDY 2

CHEM 112701

Brodifacoum

§163-1

FORMULATION--00--ACTIVE INGREDIENT

STUDY ID 42568301

Jackson, R., and B.E. Hall. 1992. Aged soil leaching of [<sup>14</sup>C]brodifacoum. Laboratory Project ID: 381986. Unpublished study performed by Inveresk Research International, Tranent, Scotland, and submitted by ICI Americas Inc., Wilmington, DE.

DIRECT REVIEW TIME = 9

REVIEWED BY: L. Parsons  
TITLE: Staff Scientist  
ORG: Dynamac Corporation  
Rockville, MD  
TEL: 301-417-9800

APPROVED BY: D. Edelstein  
TITLE: Soil Scientist  
ORG: EFGWB/EFED/OPP  
TEL: 703-305-5935

SIGNATURE:

### CONCLUSIONS:

#### Mobility - Leaching and Adsorption/Desorption

1. This study can be used towards the fulfillment of data requirements.
2. Based on column leaching experiments, aged (30 days) brodifacoum residues (89-97% as brodifacoum) were relatively immobile in columns of sand, sandy clay loam, silty clay, or clay soils that were leached with 20 inches of 0.01 M calcium chloride solution. Following leaching, 78.81-94.87% of the applied radioactivity remained in the layer of aged soil and  $\leq 0.32\%$  was recovered in the leachate. No degradates were identified in the soil or leachate.
3. This study is acceptable and partially fulfills EPA Data Requirements for Registering Pesticides by providing information on the mobility (column leaching) of ring-labeled brodifacoum residues in columns of sand, sandy clay loam, silty clay, and clay soils. However, because so little degradation was observed, this study will be considered as fulfilling the unaged mobility data requirement. Additional data will



be needed on the mobility of brodifacoum degradates in order to satisfy the aged mobility data requirement.

4. No additional information on the mobility of aged ring-labeled [<sup>14</sup>C]brodifacoum residues is required at this time. Additional data on the mobility of aged residues may be required upon the receipt of an acceptable aerobic metabolism study in which degradates of [<sup>14</sup>C]brodifacoum are identified.

#### METHODOLOGY:

Sieved (2 mm), moistened (75% of field capacity) clay, silty clay, sandy clay loam, and sand soils from Great Britain (Appendix 5) were weighed (50 g dry weight) into Erlenmeyer flasks and treated with approximately 21 ug (0.41-0.43 ppm) of [<sup>14</sup>C]brodifacoum (3-[3-(4'-bromobiphenyl-4-yl)-1,2,3,4-tetrahydro-1-naphthyl]-4-hydroxycoumarin; labeled in the phenyl ring of the hydroxycoumarin moiety; radiochemical purity >98.09%, specific activity 45.86 uCi/mg, ICI), dissolved in acetonitrile. The flasks were connected to individual continuous air-flow systems; humidified, CO<sub>2</sub>-free air was drawn through a flask, then through two tubes of ethanolamine trapping solution. The samples were incubated in the dark at 21 ± 2 C and moistened to 75% of 0.3 bar for 30 days. The trapping solutions were collected and replaced with fresh medium at various intervals during the incubation.

Subsamples of the aged treated soils were extracted twice by shaking with methylene chloride:methanol (4:1; v:v). Portions of the extracted soils were analyzed for unextracted radioactivity using LSC following combustion. An aqueous layer that formed during the first methylene chloride:methanol extraction was analyzed using LSC. The two methylene chloride:methanol extracts were combined, and aliquots were analyzed using LSC. Additional aliquots of the methylene chloride:methanol extracts were evaporated to dryness under a stream of nitrogen, and the resulting residues were redissolved in acetone. Aliquots of the acetone solutions were analyzed for total radioactivity using LSC and for specific compounds using one-dimensional TLC on silica gel plates developed in chloroform (100%). [<sup>14</sup>C]Residues on the plates were located and quantified using a linear scanner, and were identified by comparison to the location of unlabeled brodifacoum and 4-hydroxycoumarin reference standards that had been cochromatographed with the samples and located using UV (254 nm) detection. In order to confirm the results of the TLC analysis, aliquots of the soil extracts were further analyzed by HPLC using an Apex Silica 5 um column with a mobile phase of hexane:methylene chloride:acetic acid (75:25:0.6, v:v:v), and with UV (254 nm) and radioactivity detection. [<sup>14</sup>C]Residues in the HPLC eluate were quantified by LSC and identified by comparison of the retention times of nonradiolabeled cis- and trans-brodifacoum.

Duplicate glass columns (5-cm id, 42-cm height) were packed to a height of 30 cm with untreated, air-dried, sieved (2 mm) soils; the columns were "agitated gently" during packing. The soil in each column was saturated from the bottom with a 0.01 M calcium chloride solution. Portions of the aged, treated soil was then transferred to the top of the columns of the corresponding soil type. The soil columns were leached with 20 inches (1000 mL) of a 0.01 M calcium chloride solution in 48 hours; a Hoffman clip located at the bottom of each column controlled infiltration rate, and a layer of solution constantly covered the upper soil column surface throughout the leaching period. The leachate was collected continuously in amber glass containers. Following leaching, the surface segment (the layer of aged soil) of each soil column was removed and the remainder of the column was divided into 5-cm segments.

Aliquots of the column leachates were analyzed using LSC. The soil segments were mixed, and subsamples were analyzed by LSC following combustion. The surface segment from the clay, silty clay, and sandy clay loam soil columns, and the top two segments from the sand soil columns were extracted twice by shaking with methylene chloride:-methanol (4:1; v:v), and the extracts were analyzed using LSC, TLC, and HPLC as previously described for the aged treated soil. Portions of the extracted soils were analyzed using LSC following combustion.

Aliquots of the trapping solutions used during aging were analyzed using LSC. The incubation flasks used during aging and the glass columns used during leaching were rinsed with acetone, and the rinsates were analyzed by LSC.

#### DATA SUMMARY:

Aged [ $^{14}\text{C}$ ]brodifacoum residues were relatively immobile in columns (approximately 30-cm length) of British sand, sandy clay loam, silty clay, and clay soils that were topped with approximately 21 ug of aged [ $^{14}\text{C}$ ]residues (approximately 89-97% as brodifacoum; Table 6) and leached with 20 inches of a 0.01 M calcium chloride solution during a 48-hour period. Following leaching, 78.81-96.87% of the applied radioactivity remained in the layer of aged soil and  $\leq 0.32\%$  was recovered in the leachate (Table 2). The majority of the [ $^{14}\text{C}$ ]residues in the leached aged soil layer was [ $^{14}\text{C}$ ]brodifacoum; two other [ $^{14}\text{C}$ ]compounds, degradates "A" and "B", were present at up to 2.80 and 7.89% of the applied but were not identified (Table 7). Prior to use in the leaching experiments, the soils had been treated at 0.41-0.43 ppm with [ $^{14}\text{C}$ ]brodifacoum (3-[3-(4'-bromobiphenyl-4-yl)-1,2,3,4-tetrahydro-1-naphthyl]-4-hydroxycoumarin; labeled in the phenyl ring of the hydroxycoumarin moiety; radiochemical purity >98.09%) and incubated in the dark at  $21 \pm 2^\circ\text{C}$  and moistened to 75% of 0.3 bar for 30 days.

In duplicate sand soil columns, 79.47 and 94.86% of the applied radioactivity remained in the top soil segment, 2.00-4.73% was in the

5-cm segment directly below the layer of aged soil, and  $\leq 0.73\%$  was in each of the deeper 5-cm segments (Table 4). All [ $^{14}\text{C}$ ]residues in the top soil segment were cis- or trans-[ $^{14}\text{C}$ ]brodifacoum, at a ratio of approximately 41:51 (Table 7). [ $^{14}\text{C}$ ]Residues in the leachate were 0.24-0.32% of the applied, and an additional 0.30-0.96% was recovered in an acetone wash of the glass column walls (Table 2). The material balance for the columns was 89.33 and 99.59% of the applied.

In duplicate sandy clay loam soil columns, 85.76 and 85.97% of the applied remained in the top soil segment, 0.14-0.52% was in the 5-cm segment directly below the layer of aged soil, and  $\leq 0.77\%$  was in each of the deeper 5-cm segments (Table 4). In the top soil segment, cis- and trans-[ $^{14}\text{C}$ ]brodifacoum totaled 87.92-92.24% of the recovered (ratio approximately 51:39), degradate "A" was 1.50-2.80%, and degradate "B" was 3.44-4.33% (Table 7). [ $^{14}\text{C}$ ]Residues in the leachate were 0.03-0.05% of the applied, and an additional 0.09-0.17% was recovered in an acetone wash of the glass column walls (Table 2). The material balance for the columns was 91.64 and 91.75% of the applied.

In duplicate silty clay soil columns, 78.45 and 86.44% of the applied remained in the top soil segment, 0.15-0.17% was in the 5-cm segment directly below the layer of aged soil, and  $\leq 0.10\%$  was in each of the deeper 5-cm segments (Table 4). In the top soil segment, cis- and trans-[ $^{14}\text{C}$ ]brodifacoum totaled 83.79-88.44% of the recovered (ratio approximately 48:38), degradate "A" was 2.48-2.57%, and degradate "B" was 2.52-7.89% (Table 7). [ $^{14}\text{C}$ ]Residues in the leachate were 0.13-0.21% of the applied, and an additional 0.22-0.25% was recovered in an acetone wash of the glass column walls (Table 2). The material balance for the columns was 84.87 and 92.87% of the applied.

In clay soil columns, 79.19 and 83.65% of the applied remained in the top soil segment, 0.25-0.65% was in the 5-cm segment directly below the layer of aged soil, and, with the exception of 0.97% in the 10- to 15-cm deep segment,  $\leq 0.17\%$  was in each of the deeper 5-cm segments (Table 4). In the top soil segment, cis- and trans-[ $^{14}\text{C}$ ]brodifacoum totaled 91.09-91.62% of the recovered (ratio approximately 44:47; Table 7). Degradates "A" and "B" were 1.96 and 3.15% of the recovered, respectively, in the top soil segment from one column and were not detected in the second column. [ $^{14}\text{C}$ ]Residues in the leachate were 0.07-0.14% of the applied, and an additional 0.21-0.52% was recovered in an acetone wash of the glass column walls (Table 2). The material balance for the columns was 85.09 and 87.24% of the applied.

Following 30 days of aging and prior to leaching, undegraded [ $^{14}\text{C}$ ]brodifacoum was 96.79-96.96% of the recovered in the sand soil, 91.16-92.27% in the sandy clay loam soil, 88.66-88.91% in the silty clay soil, and 91.21-91.64% in the clay soil (Table 6). Three degradates, "A", "B", and "C", were 1.20-2.85%, 2.70-5.26%, and 0.91-1.81% of the recovered, respectively, in the sandy clay loam, silty clay, and clay soils, but were not identified. No degradates were

recovered from aged sand soil. At 30 days; an average 3.16% of the applied could not be extracted from the sand soil, 7.38-8.57% could not be extracted from the sandy clay loam and clay soils, and 11.76% could not be extracted from the silty clay soil (Table 1). Up to 5.53% of the applied was volatilized from the soil by 30 days (Table 1).

#### COMMENTS:

1. The study was carried out in British soil. Three of the four soils had organic matter contents considerably in excess of typical U.S. agricultural soils (4.1-5.5% organic matter). However, the Barassie sand contained only 0.54% organic matter. In all cases, the aged brodifacoum appeared to be immobile. Due to the consistency of these results, no additional aged column leaching studies in U.S. soils will be required at this time. However, all future soil mobility studies of brodifacoum must be carried out in U.S. soils.
2. Three unidentified [ $^{14}\text{C}$ ]degradates, designated "A", "B", and "C", were isolated from the aged soil prior to leaching at  $\leq 0.02$  ppm. Degradates "A" and "B" were also isolated in the soil columns after leaching at maximums of 2.80% and 7.89% of the applied (0.01 and 0.03 ppm), respectively. Although the concentrations of these compounds in the aged and leached soil may be too low to permit accurate identification, the  $R_f$  values of "A" and "B" on silica gel TLC plates developed with chloroform corresponds to the  $R_f$  values of compounds designated "C" and "A" in the aerobic soil metabolism study (MRID 42579401; Study 1 of this submission). The identification of "C" and "A" (and up to 7 other compounds) has been required prior to fulfillment of the aerobic soil metabolism data requirement.
3. When additional degradates are identified in the aerobic soil metabolism study, mobility data may be required for any significant degradates not evaluated in this study.
4. Variable trace amounts of radioactivity were found throughout the segments of the leached columns and in the leachates. Most of these data values were derived from measurements which were  $< 10$  dpm above background counts; therefore, their accuracy is uncertain.
5. Extracts of the leached samples and the aged soil samples were analyzed by HPLC. The HPLC analysis was not satisfactory since no degradates were recovered and all radioactivity was attributed to brodifacoum.
6. Six 50-g samples of each soil type were treated with brodifacoum and aged. After 30 days incubation, two samples were extracted to determine residues after aging and two samples were incubated further to measure volatiles for the extra 2 days of leaching. Two samples were used to determine leaching and the apparently the entire sample (50 g) was placed on the top of the untreated columns.

7. The study author states that for leachates "the limit of reliable determination" was 0.36% of the applied radioactivity for the columns of sandy clay loam, silty clay, and clay soils, and 0.34% of the applied radioactivity for columns of sand soil assuming 250 mL of leachate per fraction and a detection limit of 30 dpm per mL solution.

---

Page \_\_\_\_\_ is not included in this copy.

Pages 32 through 45 are not included in this copy.

---

The material not included contains the following type of information:

- \_\_\_\_\_ Identity of product inert ingredients.
- \_\_\_\_\_ Identity of product impurities.
- \_\_\_\_\_ Description of the product manufacturing process.
- \_\_\_\_\_ Description of quality control procedures.
- \_\_\_\_\_ Identity of the source of product ingredients.
- \_\_\_\_\_ Sales or other commercial/financial information.
- \_\_\_\_\_ A draft product label.
- \_\_\_\_\_ The product confidential statement of formula.
- \_\_\_\_\_ Information about a pending registration action.
- ☒ FIFRA registration data.
- \_\_\_\_\_ The document is a duplicate of page(s) \_\_\_\_\_.
- \_\_\_\_\_ The document is not responsive to the request.
- \_\_\_\_\_ Internal deliberative information.
- \_\_\_\_\_ Attorney-Client work product.
- \_\_\_\_\_ Claimed Confidential by submitter upon submission to the Agency.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

---

## REFERENCES

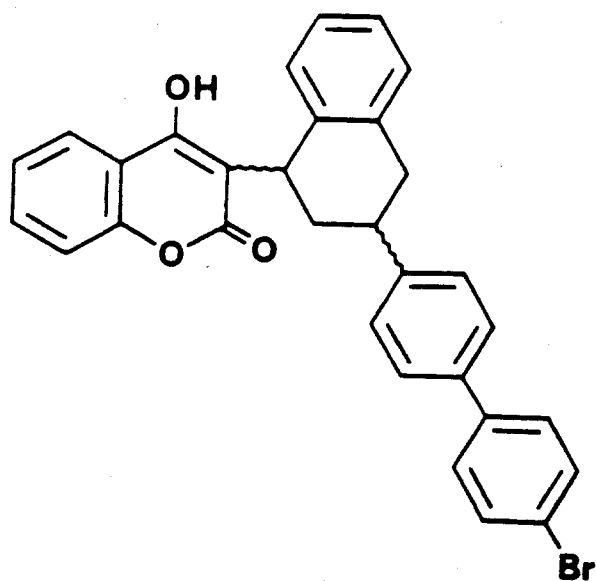
The following studies were reviewed:

Hall, B.E., and I. Priestly. 1992. Brodifacoum: Metabolism in soil under aerobic conditions. Laboratory Project ID: 381441. Unpublished study performed by Inveresk Research International, Tranent, Scotland, and submitted by ICI Americas Inc., Wilmington, DE. (42579401)

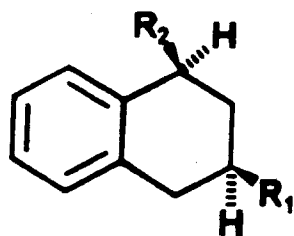
Jackson, R., and B.E. Hall. 1992. Aged soil leaching of [<sup>14</sup>C]brodifacoum. Laboratory Project ID: 381986. Unpublished study performed by Inveresk Research International, Tranent, Scotland, and submitted by ICI Americas Inc., Wilmington, DE. (42568301)

**APPENDIX**  
**BRODIFACOUM**

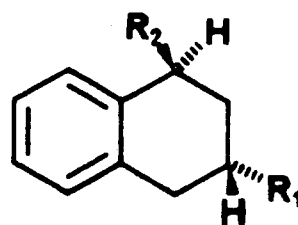




3-[3-(4'-Bromobiphenyl-4-yl)-1,2,3,4-tetrahydro-1-naphthyl]-4-hydroxycoumarin  
(Brodifacoum)



Cis Isomer



Trans Isomer

4/6

Environmental Fate & Effects Division  
PESTICIDE ENVIRONMENTAL FATE ONE LINE SUMMARY  
BRODIFACOU

Last Update on July 2, 1993

[V] = Validated Study [S] = Supplemental Study [U] = USDA Data

LOGOUT	Reviewer:	Section Head:	Date:
--------	-----------	---------------	-------

Common Name: BRODIFACOU

Smiles Code:

PC Code # : 112701

CAS #: 56073-10-0

Caswell #:

Chem. Name : 3-[3-(4'-Bromo-1,1'-biphenyl-4-yl)-1,2,3,4-tetrahydro-1-naphthyl]-4-hydroxycoumarin

Action Type: anti-coagulant

Trade Names: Talon, Havoc

(Formul'tn): garin base pellets, mini pellets, wax blocks

Physical State: off-white powder

Use : residential/industrial outdoor

Patterns :

(% Usage) :

:

Empirical Form:  $C_{31}H_{23}BrO_3$

Molecular Wgt.: 523.40

Melting Point : 228-232 C °C

Log Kow :

Henry's :

E

Atm. M3/Mol (Measured)

Vapor Pressure: 9.80E -7 Torr

Boiling Point: °C

pKa: e °C

Solubility in ...

Water

Acetone

Acetonitrile

Benzene

Chloroform

Ethanol

Methanol

Toluene

Xylene

E	ppm	@20.0 °C
E	ppm	@20.0 °C
E	ppm	e °C
E	ppm	@20.0 °C
E	ppm	@20.0 °C
E	ppm	e °C
E	ppm	e °C
E	ppm	e °C
E	ppm	e °C
E	ppm	e °C
E	ppm	e °C

Comments

<10 mg/L

6-20 g/L

0.6-6.0mg/l

3 g/L

Hydrolysis (161-1)

[ ] pH 5.0:

[ ] pH 7.0:

[ ] pH 9.0:

[ ] pH :

[ ] pH :

[ ] pH :

Environmental Fate & Effects Division  
PESTICIDE ENVIRONMENTAL FATE ONE LINE SUMMARY  
BRODIFACOU

Last Update on July 2, 1993

[V] = Validated Study [S] = Supplemental Study [U] = USDA Data

Photolysis (161-2, -3, -4)

[ ] Water:  
[ ] :  
[ ] :  
[ ] :

[ ] Soil :  
[ ] Air :

Aerobic Soil Metabolism (162-1)

[S]  $t_{1/2}$  = 157 days in sandy clay loam, pH 7.1, organic matter 4.24%

[ ]  
[ ]  
[ ]  
[ ]  
[ ]  
[ ]

Anaerobic Soil Metabolism (162-2)

[ ]  
[ ]  
[ ]  
[ ]  
[ ]  
[ ]  
[ ]

Anaerobic Aquatic Metabolism (162-3)

[ ]  
[ ]  
[ ]  
[ ]  
[ ]  
[ ]  
[ ]

Aerobic Aquatic Metabolism (162-4)

[ ]  
[ ]  
[ ]  
[ ]  
[ ]  
[ ]  
[ ]

Environmental Fate & Effects Division  
PESTICIDE ENVIRONMENTAL FATE ONE LINE SUMMARY  
BRODIFACUUM

Last Update on July 2, 1993

[V] = Validated Study [S] = Supplemental Study [U] = USDA Data

Soil Partition Coefficient (Kd) (163-1)  
[V] parent immobile in column leaching

[ ]  
[ ]  
[ ]  
[ ]  
[ ]  
[ ]

Soil Rf Factors (163-1)

[ ]  
[ ]  
[ ]  
[ ]  
[ ]  
[ ]

Laboratory Volatility (163-2)

[ ]  
[ ]

Field Volatility (163-3)

[ ]  
[ ]

Terrestrial Field Dissipation (164-1)

[ ]  
[ ]  
[ ]  
[ ]  
[ ]  
[ ]  
[ ]  
[ ]  
[ ]  
[ ]

Aquatic Dissipation (164-2)

[ ]  
[ ]  
[ ]  
[ ]  
[ ]  
[ ]

Forestry Dissipation (164-3)

[ ]  
[ ]

Environmental Fate & Effects Division  
PESTICIDE ENVIRONMENTAL FATE ONE LINE SUMMARY  
BRODIFACUUM

Last Update on July 2, 1993

[V] = Validated Study    [S] = Supplemental Study    [U] = USDA Data

Long-Term Soil Dissipation (164-5)

[ ]  
[ ]

Accumulation in Rotational Crops, Confined (165-1)

[ ]  
[ ]

Accumulation in Rotational Crops, Field (165-2)

[ ]  
[ ]

Accumulation in Irrigated Crops (165-3)

[ ]  
[ ]

Bioaccumulation in Fish (165-4)

[ ]  
[ ]

Bioaccumulation in Non-Target Organisms (165-5)

[ ]  
[ ]

Ground Water Monitoring, Prospective (166-1)

[ ]  
[ ]  
[ ]  
[ ]

Ground Water Monitoring, Small Scale Retrospective (166-2)

[ ]  
[ ]  
[ ]  
[ ]

Ground Water Monitoring, Large Scale Retrospective (166-3)

[ ]  
[ ]  
[ ]  
[ ]

Ground Water Monitoring, Miscellaneous Data (158.75)

[ ]  
[ ]  
[ ]

Environmental Fate & Effects Division  
PESTICIDE ENVIRONMENTAL FATE ONE LINE SUMMARY  
BRODIFACOU

Last Update on July 2, 1993

[V] = Validated Study [S] = Supplemental Study [U] = USDA Data

Field Runoff (167-1)

[ ]  
[ ]  
[ ]  
[ ]

Surface Water Monitoring (167-2)

[ ]  
[ ]  
[ ]  
[ ]

Spray Drift, Droplet Spectrum (201-1)

[ ]  
[ ]  
[ ]  
[ ]

Spray Drift, Field Evaluation (202-1)

[ ]  
[ ]  
[ ]  
[ ]

Degradation Products

several isolated, none identified yet

Environmental Fate & Effects Division  
PESTICIDE ENVIRONMENTAL FATE ONE LINE SUMMARY  
BRODIFACOU

Last Update on July 2, 1993

[V] = Validated Study [S] = Supplemental Study [U] = USDA Data

Comments

Appears to be relatively persistent (aerobic soil half-life = 157 days). Parent immobile. Major degradates still unidentified. Behavior in sterile aqueous solution still unknown.

References:

Writer : DME